## REMARKS

Reconsideration is requested.

Claims 1-66 have been canceled, without prejudice.

Claim 67 is pending.

The objection to claim 46 is moot in view of the above.

The Section 112, second paragraph, rejections of claims 32 and 46 are moot in view of the above.

The following art rejections are moot in view of the above:

The Section 103 rejection of claims 31, 32, 37-42, 44, 46 and 57-66 over Cameron (U.S. Patent No. 4,722,837), JP 07-18946 (Hirota), The Handbook of Cosmetic Science and Technology and U.S. Patent No. 5,998,395 (Kligman);

The Section 103 rejection of claim 55 over Cameron, Hirota, The Handbook of Cosmetic Science and Technology, Kligman and U.S. Patent No. 5,378,731 (Andrews);

The Section 103 rejection of claims 52-54 and 56 over Cameron, Hirota, The Handbook of Cosmetic Science and Technology, Kligman and U.S. Patent No. 5,661,118 (Cauwet);

The Section 103 rejection of claims 31-32, 37-42, 44, 46, 55 and 57-66 over Kligman and Su (U.S. Patent No. 4,329,334); and

The Section 103 rejection of claims 52-54 and 56 over Kligman, Su and Cauwet.

The Section 103 rejection of claim 67 over Kligman (U.S. Patent No. 5,998,395), Su (U.S. Patent No. 4,329,334), Cameron (U.S. Patent No. 4,722,837), Cauwet (U.S. Patent No. 5,661,118) and U.S. Patent No. 5,631,003 (Mueller), is traversed.

Reconsideration and withdrawal of the rejection are requested in view of the following and the attached.

The Examiner has failed to establish a *prima facie* case of obviousness of the invention of claim 67.

As noted by the Federal Circuit in In re Fritch, , 23 USPQ2d 1780, 1783-1784 (Fed. Cir. 1992)

> "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so." [ACS Hosp. Systems, Inc. v. Montefiore Hosp ., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed.Cir. 1984).] Although couched in terms of combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious "modification" of the prior art. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. [In re Gordon, 733 F.2d at 902, 221 USPQ at 1127.] Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board.

The Federal Circuit similarly noted the following in In re Mills, 16 USPQ2d 1430, 1432 (Fed. Cir. 1990):

> While Mathis' apparatus may be capable of being modified to run the way Mills' apparatus is claimed, there must be a suggestion or motivation in the reference to do so. See In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed.Cir. 1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.").

For the reasons detailed below, the applicants submit that the Examiner has not indicated where the cited art motivated one of skill in the art to have made the claimed composition or where the purported obvious modification of the five (5) cited references to make the claimed invention is suggested by the art. As further noted below, modification of at least one of the cited reference (i.e., Kligman) would have, in the applicants view, been contrary to the teaching of the reference.

The Examiner's combination of cited art has been made with an impermissible use of hindsight. The Examiner has failed to establish a *prima facie* case of obviousness. Withdrawal of the Section 103 rejection is requested.

One of ordinary skill in the art would not have anticipated success in making the claimed composition, with the advantageous properties inherent to the claimed composition, from the cited art.

Moreover, as further detailed below, (a) increasing the amount of alcohol over the amount provided in the teaching of Su would have been contrary to the teaching of the reference, (b) making a composition of clobetasol propionate in the absence of tretinoin (as claimed) would have been contrary to Kligman, (c) the claimed composition has been previously demonstrated to be patentable over Cameron combined with a reference allegedly teaching use of 10% ethanol, and (d) the mere fact that surface active agents and polymers containing cationic groups and pH regulators could be used in shampoos, such as are used in compositions of Cauwet and Mueller, would not have made their combination in the claimed composition obvious.

The Examiner is understood to believe that the composition of claim 67 would have been obvious to one of ordinary skill in the art because Kligman teaches a

composition containing clobetasol propionate in an amount of 0.05% (see pages 7 and 21 of the Office Action dated May 3, 2007), Su teaches a composition containing 65-80% water, 0.1-7.5% amphoteric surfactant and "can contain an alcohol that is ethanol to improve cleansing" (see page 21 of the Office Action dated May 3, 2007), Cameron teaches "that shampoo compositions can contain detergents such as sodium lauryl sulfate and sodium laureth sulfate" (see page 22 of the Office Action dated May 3, 2007), Cauwet "teaches a hair washing composition (shampoo) comprising surface active agents and polymers containing cationic groups, to give a conditioning effect to hair" (see page 23 of the Office Action dated May 3, 2007) and Mueller "teaches that typical constituents of hair preparations include pH regulators, such as a citric acid/sodium citrate buffer" (see, page 25 of the Office Action dated May 3, 2007).

By the Examiner's own characterization, Kligman teaches that Kligman's composition of clobetasol propionate and tretinoin "work synergistically". See page 7 of the Office Action dated May 3, 2007. It would have been contrary to the teachings of Kligman to have made a composition of the claimed invention, which does not include tretinoin, as Kligman requires the presence of tretinoin for the "synergistic effect" recognized by the Examiner. Kligman therefore teaches away from the presently claimed invention. None of Su, Cameron, Cauwet and/or Mueller cure this deficiency of Kligman.

Su teaches a composition which contains the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one (see column 3, lines 1-15 and the claims of Su) with

> "essential anionic and amphoteric components [which] ... comprise an anionic sulfate or sulfonate surfactant, an amphoteric surfactant such as the betaine or sulfobetaine or amidobetaine or amidosulfobetaine, a higher fatty acid ethanolamide and preferably a nonionic surfactant selected from the group consisting of a tertiary amine oxide and/or a polyethoxylated hexitan fatty acid ester and a lower aliphatic mono- and/or polyhydric alcohol in certain critical amounts in order to avoid precipitation of the antimicrobial agent." See column 4, lines 8-18 of Su.

The critical amount of "a lower aliphatic monohydric and/or polyhydric alcohol" is "about 0.5-2% by weight". See column 4, lines 16-18 and 33-35 of Su.

The present claimed composition does not include the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one such that one of ordinary skill in the art, following Su, would not have been motivated to include a lower aliphatic monohydric and/or polyhydric alcohol in a composition containing any other ingredients of Su's composition. That is, the motivation of Su in including about 0.5-2% by weight of a lower aliphatic monohydric and/or polyhydric alcohol was to avoid precipitation of the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one. If one of ordinary skill in the art were to make a composition which did not contain the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one then that person of ordinary skill in the art would not have been motivated by Su to include about 0.5-2% by weight of a lower aliphatic monohydric and/or polyhydric alcohol.

Further, making a shampoo composition which lacks the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one would be contrary to Su as the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one is a critical component of the composition. The claimed composition, which does not

include the antimicrobial agent 1-imidazolyl-1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one would have been contrary to, and not obvious from the teachings of Su.

Finally, the amount of alcohol in Su's composition (i.e., about 0.5-2% by weight of a lower aliphatic monohydric and/or polyhydric alcohol) is a "critical" amount. As such, altering the amount of alcohol above the critical amount "to improve cleansing" (see page 21 of the Office Action dated May 3, 2007) would be contrary to the teaching of a critical aspect of Su. While Su teaches at column 6, lines 42-52, that inclusion of the lower aliphatic alcohol component enhances cleansing. Su does not teach in this passage, or elsewhere, that the critical amount of about 0.5-2% by weight of a lower aliphatic monohydric and/or polyhydric alcohol should be exceeded "to improve cleansing".

For completeness, the applicants note that Su teaches the inclusion of an ethanolamide component (see above-quoted passage as well as column 6, lines 34-41 of Su) as a foam booster. The required or preferred ethanolamide component of Su is not included in the presently claimed composition. Su fails to teach or suggest the exclusion of an ethanolamide component from a shampoo composition. Exclusion of an ethanolamide component from a shampoo would be contrary to Su.

Further, Su does not teach of suggest increasing the amount of alcohol taught by Su "to improve cleansing". In fact, Su teaches that the "cleansing" of the shampoo of Su is provided by anionic sulfate or sulfonate surface active agents

The teachings of Kligman, Cameron, Cauwet and Mueller fail to cure these deficiencies of Su.

The pending claim has been demonstrated to be patentable over Cameron in combination with Hirota which allegedly teaches an amount of alcohol required by the claims. The applicants have previously demonstrated that

> "the addition of ethanol to a composition that falls within the preferred embodiment of Cameron results in a composition having a substantially reduced viscosity and foaming capability. As Cameron clearly teaches the desirability of providing foam stabilizers to give a foaming composition (see column 2, lines 40-55, in particular), it is considered that one of ordinary skill in the art would not have found it obvious, based on the teachings of Cameron, to provide an ingredient that appears to significantly reduce the foaming capabilities and viscosity of the composition." See pages 2-3 of the Office Action dated May 3, 2007.

As noted above, Kligman, which teaches a composition containing clobetasol propionate, would not have made the claimed invention obvious and that to have made the claimed invention would have been contrary to Kligman.

The claimed invention is patentable over Cameron for the reasons noted by the Examiner. The Examiner's selective reliance on Cameron for a teaching of detergents in shampoo compositions fails to consider the whole of the cited art. See for example, Medichem S.A. v. Rolabo S.L., 77 USPQ2d 1865, 1871 (Fed. Cir. 2006) ( "the prior art must be considered as a whole for what it teaches"); and In re Paulsen, 31 USPQ2d 1671 (Fed. Cir. 1994) ("we have been guided by the well-settled principles that the claimed invention must be considered as a whole, multiple cited prior art references must suggest the desirability of being combined, and the references must be viewed without the benefit of hindsight afforded by the disclosure. See Hodosh v. Block Drug Co., Inc. , 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed.Cir.), cert. denied , 479 U.S. 827 (1986)." ).

Considered as a whole, Cameron fails to suggest the claimed invention.

The combination of Kligman, Su, Cauwet and Mueller fail to cure the deficiencies of Cameron.

Finally, the applicants submit that the existence of cosmetic ingredient in the teachings of Cauwet and Mueller selected by the Examiner would not have made the claimed composition obvious in view of Kligman, Su and Cameron. The mere existence of components of the claims in the art would not have made there combination obvious without some motivation and suggestion to have made the claimed combination.

The claimed invention is submitted to be patentable over the cited combination of art. The Examiner is not believed to have established a *prima facie* case of obviousness. Withdrawal of the Section 103 rejection of claims 67 is requested.

While not believed to be required, the Examiner is further requested to see the attached further PREUILH Declaration which demonstrates that a composition 1 (containing 2% of alcohol) presents an opaque appearance due to crystals of Clobetasol-17-propionate and that, upon microscopic observation, the opaque appearance of the composition 1 (containing 2% of alcohol) increases with the number of crystals of Clobetasol-17-propionate. The attached further provides results obtained with Clobex® Shampoo show that the addition of 10% of alcohol permits one to obtain a clear shampoo without crystals. The presence of crystals in composition 1 demonstrates that 2% of alcohol is not enough to obtain a good solubilization of 0.05% of Clobetasol-17-propionate and therefore a good stability of the resulting composition.

Consideration of the attached further Declaration is requested.

Withdrawal of the Section 103 rejection of claim 67 is requested.

The application is submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required to place the application in condition for allowance.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | |
|---|---|---|
| In re Application of: | ) | |
| | ) | |
| **Isabelle PREUILH et al.** | ) | |
| | ) | |
| Application No.: 09/709,477 | ) | Group Art Unit: 1617 |
| | ) | |
| Filed: November 13, 2000 | ) | Examiner: A.M. COTTON |
| | ) | |
| For: FOAMING COMPOSITIONFOR TREATING THE HAIR | ) | |
| | ) | Confirmation No. 4547 |
| | ) | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

**DECLARATION UNDER 37 C.F.R. § 1.132**

I, Isabelle PREUILH, declares and states that,

- I am a French citizen residing at 12 rue des Moulieres –Elegancia C – O6110 le Cannet, FRANCE ;
- I am a Doctor in Pharmacy graduate from the University of Pharmacy in Bordeaux
- I am employed by GALDERMA as a pharmaceutical project manager and have experience working with hair care compositions ;
- At the time of the invention I was Head of Formulation group at Galderma R&D
- I am a named inventor and am familiar with the United States patent application No. 10/709,477 filed on November 13, 2000, for FOAMING COMPOSITION FOR TREATING THE HAIR ;
- I have read and am familiar with the prior art references cited by the Examiner, and more particularly Su et al (U.S. Patent No. 4,329,334),
- given my education and experience, particularly in the area of hair care, I consider myself able to provide the following testimony based on experiments conducted or under my supervision:

## Comparative tests

The shampoo sold under the trade name Clobex® Shampoo, which composition corresponds to that of example VIII of the invention (comprising 10% of alcohol), has been compared to a shampoo composition comprising the same ingredients but with 2% of alcohol.

1. **Comparison of the shampoo according to our US patent application No. 10/709,477 to a clobetasol shampoo**

### 1.1 Presentation of the formulas

The table 1 represents the 2 tested formulas one with 10% of alcohol (Clobex Shampoo® = Ex VIII) and a second with 2% of alcohol ( = Composition 1 in which the concentration of alcohol corresponds to the concentration of alcohol in Su et al). I have evaluated the influence of alcohol on the solubility of the drug substance.

| Number of the raw material | Function | Trade name | INCI name | Quantity (%) (Ex VIII) | Quantity (%) (Composition 1) |
|---|---|---|---|---|---|
| 1 | pH adjuster | Citric acid monohydrate | | 0.24 | 0.24 |
| 2 | pH adjuster | Sodium citrate USP 2H2O[(1)] | Sodium citrate dihydrate | 2.6 | 2.6 |
| 3 | Thickener | Celquat SC240C[(2)] | Polyquaternium 10 | 2.0 | 2.0 |
| 4 | Anionic surfactant | Texapon N70[(3)] | Sodium lauryl ether sulfate | 17.0 | 17.0 |
| 5 | Amphoteric surfactant | Dehyton AB30[(3)] | Cocoyl betaine | 6.0 | 6.0 |
| **6** | **Propenetrating agent and solvent of the active drug** | **Ethanol 95/96** | **Alcohol** | **10.0** | **2.0** |

| | | | | | |
|---|---|---|---|---|---|
| 7 | Drug substance | Clobetasol-17-propionate | | 0.05 | 0.05 |
| 8 | Vehicle | Purified water | Aqua | Qsp 100% | Qsp 100% |

Table 1: Presentation of Clobex Shampoo's formulas

(1) sold by COOPER
(2) sold by National Starch & Chemical
(3) sold by Cognis

### 1.2 Characteristics of Clobex® Shampoo's formulas

The two clobetasol shampoos are realised and placed at 4°C and at room temperature to follow the evolution of the formulas in the time at macroscopic and microscopic level.

#### *1.2.1 Macroscopic appearance of the formulas*

The table 2 below describes the different observations which are carried out on the two formulas:

| | **Clobex® Shampoo (Ex VIII of the invention with 10% of alcohol)** | | **Composition 1 ( with 2% of alcohol)** | |
|---|---|---|---|---|
| | **Room temperature** | **4°C** | **Room temperature** | **4°C** |
| T= 0 | A lot of bubbles air (normal due to stirring) | | A lot of bubbles air (normal due to stirring) | |
| T= +24h | Clear liquid | Clear liquid | Unclear liquid | Unclear liquid |
| T= +48h | Clear liquid | Clear liquid | Unclear liquid | Unclear liquid |
| T= +1 week | Clear liquid | Clear liquid | Liquid more opaque than at T= +48h | Liquid more opaque than at T= +48h |

| | | | | |
|---|---|---|---|---|
| T= +2 weeks | Clear liquid | Clear liquid | Liquid more opaque than at T= +48h | Liquid more opaque than at T= +48h |

Table 2: Appearance of the formulas

Only composition 1 (with 2% of alcohol) presents an opaque appearance. This opaque appearance is known to be due to the presence of Clobetasol-17-propionate crystals in the composition due to the low content of ethanol (2% w/w). This conclusion has been confirmed with microscopic observations in a second step.

*1.2.2 Microscopic observations*

Different microscopic observations in various conditions of temperature and time (cf table 3) are carried out (with the Zeiss microscope, polarized light) in order to check if crystallisation of the drug substance takes place in the formulas.

| | **Time** | **Storage condition** | **Formulas** |
|---|---|---|---|
| Table 4 | T0 | Room temperature | Composition 1 |
| Table 5 | T0 | Room temperature | Clobex Shampoo |
| Table 6 | 3 days | 4°C | Composition 1 |
| Table 7 | 5 days | 4°C | Composition 1 |
| Table 8 | 5 days | 4°C | Clobex Shampoo |
| Table 9 | 2 weeks | 4°C | Composition 1 |
| Table 10 | 2 weeks | Room temperature | Composition 1 |
| Table 11 | 2 weeks | 4°C | Clobex Shampoo |
| Table 12 | 2 weeks | Room temperature | Clobex Shampoo |

Table 3: Conditions of the microscopic observations

Tables 4, 5, 6, 7, 8, 9, 10, 11, 12, below show the results:

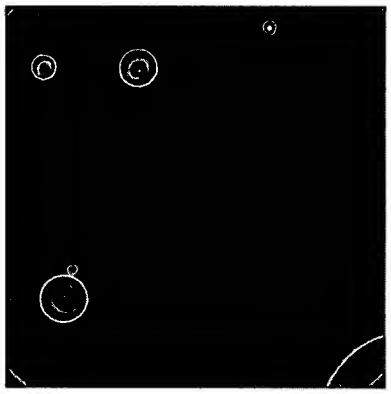
| | |
|---|---|
| **Composition 1**<br>Room temperature; T0<br>Enlargement = 240<br><br>**Macroscopic appearance:** a lot of bubbles air (normal due to stirring)<br>**Comments:** No crystals. |  |

Table 4: Composition 1 (with 2% of alcohol)

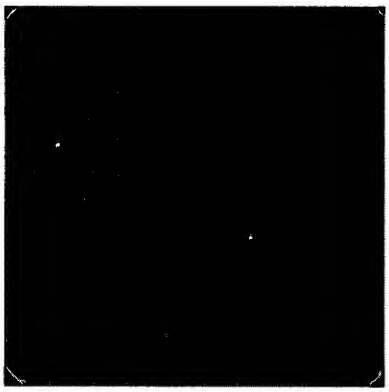
| | |
|---|---|
| **Clobex® Shampoo (ex VIII)**<br>Room temperature; T0<br>Enlargement = 240<br>**Macroscopic appearance:** a lot of bubbles air (normal due to stirring)<br>**Comments:** No crystals. |  |

Table 5 : Clobex Shampoo (ex VIII)

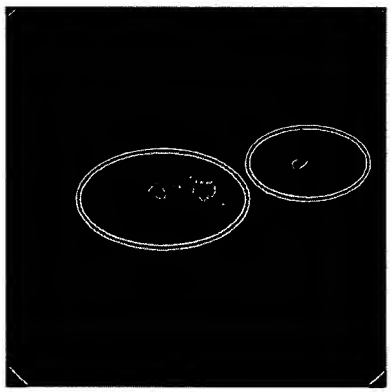
| | |
|---|---|
| **Composition 1**<br>4°C; 3 days<br>Enlargement = 600<br><br>**Macroscopic appearance:** unclear liquid<br><br>**Comments:** Crystals of Clobetasol-17-propionate.<br>Average diameter of the crystals = 5µm |  |

Table 6: Composition 1 (with 2% of alcohol)

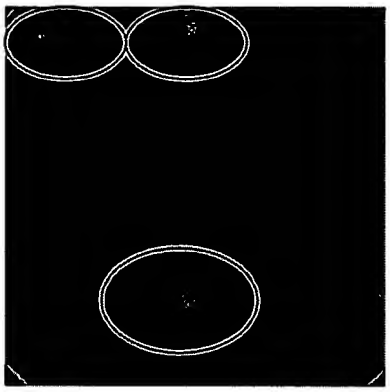
| | |
|---|---|
| **Composition 1**<br>4°C; 5 days<br>Enlargement = 240<br><br>**Macroscopic appearance:** unclear liquid<br><br>**Comments:** Crystals of Clobetasol-17-propionate.<br>Average diameter of the crystals = 15µm |  |

Table 7: Composition 1 (with 2% of alcohol)

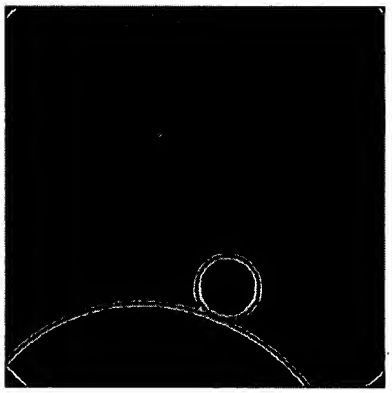
| | |
|---|---|
| **Clobex® Shampoo (ex VIII)**<br>4°C; 5 days<br>Enlargement = 240<br><br>**Macroscopic appearance:** clear liquid<br><br>**Comments:** No crystals. |  |

Table 8 : Clobex Shampoo (ex VIII)

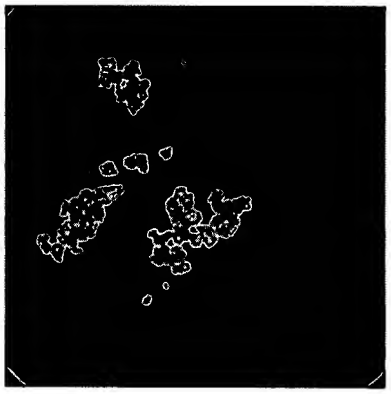
| | |
|---|---|
| **Composition 1**<br>4°C; 2 weeks<br>Enlargement = 240<br><br>**Macroscopic appearance:** unclear liquid<br><br>**Comments:** Numerous crystals of Clobetasol-17-propionate.<br>Average diameter of the crystals = 20µm |  |

Table 9: Composition 1 (with 2% of alcohol)

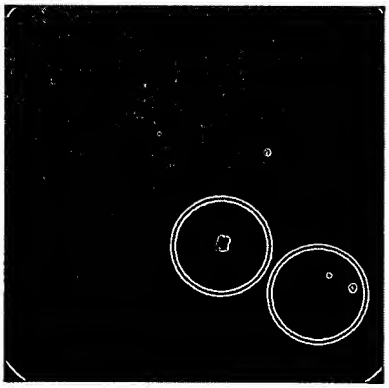
| | |
|---|---|
| **Composition 1**<br>Room temperature; 2 weeks<br>Enlargement = 240<br><br>**Macroscopic appearance:** unclear liquid<br><br>**Comments:** Crystals of Clobetasol-17-propionate.<br>Average diameter of the crystals = 15µm |  |

Table 10: Composition 1 (with 2% of alcohol)

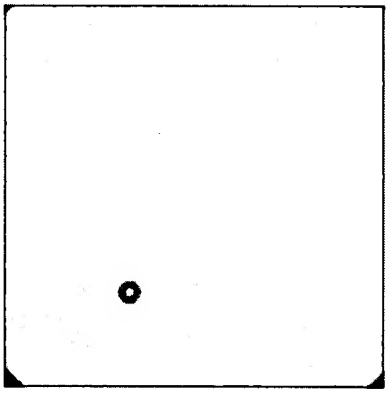
| | |
|---|---|
| **Clobex® Shampoo (ex VIII)**<br>4°C; 2 weeks<br>Enlargement = 240<br><br>**Macroscopic appearance:** clear liquid<br><br>**Comments:** No crystals. |  |

Table 11: Clobex® Shampoo (ex VIII)

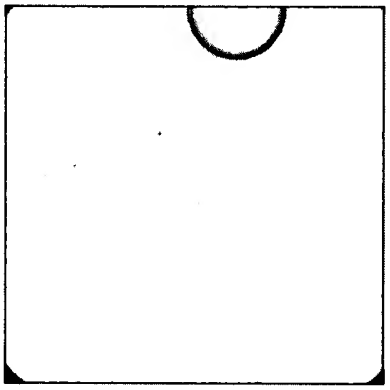
| | |
|---|---|
| **Clobex® Shampoo (ex VIII)**<br>Room temperature; 2 weeks<br>Enlargement = 240<br><br>**Macroscopic appearance:** clear liquid<br><br>**Comments:** No crystals |  |

Table 12: Clobex Shampoo (ex VIII)

Using the different microscopic observations, I have observed crystals in composition 1 as of the third day at 4°C. The presence of crystals in composition 1 is confirmed after 5 days and two

weeks at 4°C, and even at room temperature after 2 weeks. The number and the size of crystals in the composition 1 increase in the time at 4°C. Clobex® Shampoo (ex VIII) presents no crystals in all conditions of temperature and time.

### 1.3 Conclusion

The macroscopic and microscopic observations of the two formulas show that composition 1 (2% of alcohol) presents an opaque appearance due to crystals of Clobetasol-17-propionate. Results obtained with Clobex® Shampoo show that the addition of 10% of alcohol permits to obtain a clear shampoo without crystal. The presence of crystals in composition 1 proves that 2% of alcohol, as teached in Su et al's patent, is not sufficient to obtain a good solubilization of Clobetasol-17-propionate and therefore a good stability of the resulting composition. Indeed, Clobetasol-17-propionate crystallise over time both at 4°C and room temperature.

I further declare that all statements made herein of my own knowledge are true and that all statements are made on information and belief are believed to be true ; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 20 July 2007 By: _____
Isabelle PREUILH